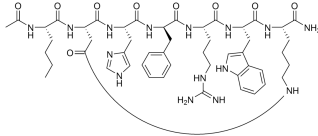


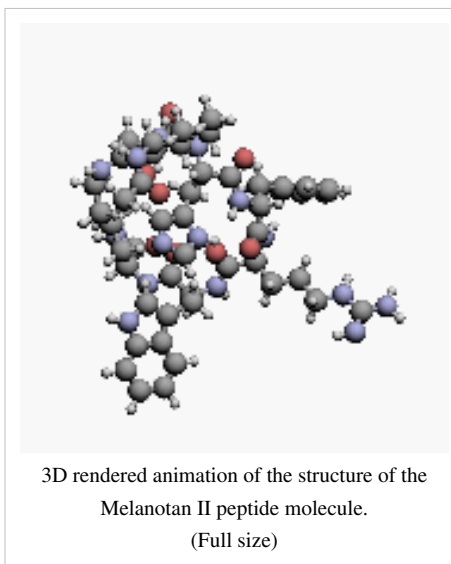
Melanotan II

Melanotan II	
	
Identifiers	
CAS number	121062-08-6 ^[1] ✓
PubChem	92432 ^[2]
ChemSpider	83450 ^[3] ✓
MeSH	melanotan-II ^[4]
ChEMBL	CHEMBL430239 ^[5] ✓
IUPHAR ligand	1323 ^[6]
Properties	
Molecular formula	C ₅₀ H ₆₉ N ₁₅ O ₉
Molar mass	1024.180
✗ (verify) ^[7] (what is: ✓ / ✗ ?)	
Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)	
Infobox references	

Note: this article describes melanotan II which should not be confused with melanotan-I which is also known by the generic name afamelanotide.

Melanotan II (ⁱ/mɛˈlænətæn/) developed at the University of Arizona is a synthetic analog of the naturally occurring melanocortin peptide hormone alpha-melanocyte stimulating hormone (α -MSH) that in usage has been shown to have melanogenesis (tanning) and aphrodisiac effects in preliminary studies and clinical trials.^{[8][9][10]} It is a cyclic lactam analog of α -MSH with the amino acid sequence Ac-Nle-cyclo[Asp-His-D-Phe-Arg-Trp-Lys]-NH₂.

As of 2010 no compound incorporating the melanotan II peptide has ever been approved for use by any governmental drug regulatory bodies outside of clinical trials. Unlicensed and untested powders sold as "melanotan II" are found on the Internet^[11] and are reported to be used by thousands of members of the general public. Multiple regulatory bodies have warned consumers the peptides may be unsafe and ineffective in usage with one regulatory agency warning that consumers who purchase any product labeled "melanotan" risk buying a counterfeit drug.^[12] Medical researchers and Clinuvel Pharmaceuticals, the company developing the related peptide afamelanotide, has warned consumers that counterfeit products sold using the names "melanotan I and II", "pose a hazard to public health".^[13]



Historical development

Melanotan II was first synthesized at the University of Arizona. Researchers there knew that one of the best defenses against skin cancer was melanin activated in the skin, a tan. They hypothesized that an effective way to reduce skin cancer rates in people would be to induce the body's natural pigmentary system to produce a protective tan prior to UV exposure. The body's naturally occurring hormone α -MSH causes melanogenesis, a process by which the skin's pigment cells (melanocytes) produce the skin's pigment (melanin). They tested to see if administering this endogenous hormone to the body directly could be an effective method to cause sunless tanning. What they found was that while it appeared to work, natural α -MSH had too short a half life in the body to be practical as a therapeutic drug. So they decided to find a more potent and stable alternative, one that would be more practical.

After synthesizing and screening hundreds of molecules, the researchers headed by Victor J. Hruby and Mac E. Hadley,^[14] found a peptide, [Nle⁴, D-Phe⁷]- α -MSH, that was approximately 1,000 times more potent than natural α -MSH.^[15] They dubbed this new peptide molecule, "Melanotan" (later Melanotan-1, now known as afamelanotide). They subsequently developed another analog, Ac-Nle-cyclo[Asp-His-D-Phe-Arg-Trp-Lys]-NH₂, which they called "Melanotan II". The scientists hoped to use these peptides to combat melanoma by stimulating the body's natural pigmentary mechanism to create a tan without first needing exposure to harmful levels of UV radiation.^[16] This in turn, they hypothesized, could reduce the potential for skin damage^{[17][18]} that can possibly lead to skin cancer.

The scientists licensed their patented peptides, via a technology transfer company, to a number of biotechnology companies who intend to develop them into drugs.^[19]

Human clinical trials

A pilot Phase I clinical trial conducted on three males by the *College of Medicine, Pharmacology Department, University of Arizona* in Tucson, Arizona published in 1996 reported that, "Melanotan II has tanning activity in humans given only 5 low doses every other day by subcutaneous injection." The side effects reported were mild nausea and a "stretching and yawning complex" that correlated with spontaneous penile erections.^[20]

The *Department of Pharmacology, University of Arizona College of Medicine* published a study in 1998 that involved ten men who suffered from psychogenic erectile dysfunction. Their trial concluded that, "Melanotan-II is a potent initiator of erections in men with psychogenic erectile dysfunction and has manageable side effects at a dose of 0.025 mg./kg."^[21]

A clinical study published in 2000 of 20 men with psychogenic and organic erectile dysfunction conducted at the *Section of Urology of The University of Arizona College of Medicine* concluded, "that Melanotan II is a potent initiator of penile erection in men with erectile dysfunction."^[22]

General population usage of melanotan peptides

General public users of the melanotan peptides have been reported to number into the thousands with one BBC report explaining that a January 2009 straw poll by the reporting journalist of just 6 UK needle exchanges revealed, "nearly 500 people wanting the syringes [for peptide usage] or information about melanotan".^{[23][24][25]} Academic researchers have reported on a "thriving" internet community of users of the peptides at the site Melanotan.org^[26] where members discuss their experiences using the unlicensed and unregulated drugs.^[27] The site was reported to number more than 5,000 members as of February 2009.^[28] A January 2009 report in Wired Science described the site's forum as having more than 50,000 posts primarily covering "Usage and Experimentation" by members with many covering detailed regimens on how to attain skin darkening and/or sexual function [with Melanotan II] improvements.^[29] In May 2010 the Norwegian tabloid daily Verdens Gang published a story based upon a report by the Norwegian Pharmacy Association stating that 10,000 syringes are sold annually to Norwegian users of melanotan-1 and melanotan II.^[30]

"Melanotan" products sold for human use

A number of products are sold online and in gyms and beauty salons as "melanotan" or "melanotan-1" which purport to have the same chemical make up as afamelanotide, of which the visual effect resulting from usage has been noted in an article by Wired.com as being "eerily similar to results obtained in trials at the University of Arizona or by Clinuvel [An Australian company trialing the related afamelanotide peptide]". The Wired.com article explained that these products were Melanotan II, "a similar (but not identical) compound"^[29] and Clinuvel has stated that products sold as "melanotan" are "illegal" and "wholly unrelated to Clinuvel's proprietary afamelanotide".^[13] Chemicals sold as "melanotan" are not illegal to import, use or own, however their domestic sales (non-export) and supply for human use outside of government sanctioned clinical trials is illegal within the boundaries of most jurisdictions, including the UK,^[23] USA, Europe and Australia.^[31]

A 2009 paper on unlicensed "melanotan" products, sold on the internet, has reported that the products caused moles to darken and increase in size over a short period, "an early warning sign of skin cancer".^{[32][33][34][35]} Academic researchers at Liverpool John Moores University specialized in performance-enhancing drugs published an editorial in the British Medical Journal suggesting that use of 'melanotan I and II', "could damage the immune and cardiovascular systems as well as triggering other problems".^[36]

Health warnings on "melanotan" products sold for human use

In 2007, the FDA issued a Warning Letter to an American online vendor illegally marketing melanotan II on the internet as a drug that prevents skin cancer and assists tanning. The FDA has not licensed melanotan II, and explained: "There is no evidence that the product is generally recognized as safe and effective [GRAS/E] for its labeled uses." The FDA concurrently gave a blanket warning advising consumers to, "stop using Melanotan II, an unapproved product".^[37]

On August 8, 2008 the Danish Medicines Agency (DMA) issued a warning^[38] against the usage of any product called "Melanotan" purchased on the internet, noting that claims that imply that it has an, "effect" for protection against skin cancer, "has not been documented". The DMA further warned that Melanotan has not undergone tests for its effect and possible side effects, and is an "illegal medicinal product" that it is not licensed for usage in the EU or the USA.

The UK Medicines and Healthcare products Regulatory Agency issued a similar warning on November 17, 2008^[39] stating that "We are warning people not to use this product. Don't be fooled into thinking that Melanotan offers a shortcut to a safer and more even tan. The safety of these products is unknown and they are unlicensed in the UK. The side effects could be extremely serious. If you have used either of these products do not use them again and if you have any concerns you should seek advice from your doctor."

The FDA issued a warning letter to another online vendor in January 2009 selling "10 MG MT 2 [Melanotan II] -American Lab" as advertisements of the products on their website were in breach of the Federal Food, Drug, and Cosmetic Act as the site was selling "new drug" products "intended for human use".^[40]

The Irish Medicines Board (IMB) issued a precautionary safety alert on February 27, 2009 regarding the use of "the unauthorised medicine Melanotan (I and II)", sold as a powder for injection, stating that "Melanotan is not authorised in Ireland and therefore the IMB cannot guarantee the efficacy, safety or quality of this product."^[11] In its release, the IMB announced that its tests had found the presence of microbial contamination in a vial of water sold together with melanotan powder which "would expose recipients to a risk of serious infection".

The Norwegian Medicines Agency has issued warnings in 2007^[41] and 2009^[12] about the use of "Melanotan" sold online, while a spokesman for the Australian Therapeutic Goods Administration warned consumers to be "very wary" of using it.^[31]

In late July 2010 the Swedish Medical Products Agency issued a warning against the usage of melanotan II.^[42]

Bremelanotide

Palatin Technologies developed another hormone targeted towards sexual dysfunction therapy based upon melanotan II called bremelanotide (formerly PT-141). Bremelanotide is a metabolite of melanotan II that lacks the C-terminal amide function. The drug has been undergoing clinical trials for the treatment of sexual arousal disorder and erectile dysfunction. It is intended for both men and women. Preliminary results have proven the efficacy of this drug,^[43] however development was briefly suspended^[44] due to a side effect of increased blood pressure observed in a small number of trial subjects administered the drug intranasally. On August 12, 2009, Palatin announced positive results (none of the previous heightened blood pressure effects were observed) of a phase I clinical study where trial subjects were instead administered the drug subcutaneously.^[45] Palatin is concurrently developing a related compound they call PL-6983.

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External links

- Melanotan.org (<http://melanotan.org/>)
- PubChem entry Melanotan II (<http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?sid=669326>)
- PubChem entry *rac*-Melanotan II (<http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?sid=10486716>) (*racemic Phe*)

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